The Difference of Predictors for Recurrence After Catheter Ablation of Non-Paroxysmal Atrial Fibrillation According to Follow-Up Period

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SUMMARY

The aim of this study was to assess the clinical and echocardiographic predictors for the recurrence of persistent atrial fibrillation (AF) after ablation during a long-term period.

A total of 130 patients with persistent AF who had undergone radiofrequency catheter ablation (RFCA) were enrolled. We analyzed the relation between clinical parameters, echocardiographic parameters, and AF recurrences at 6 months, 1 year, and 2 years after ablation.

During the 2-year follow-up, AF recurred in 61 patients (46.6%). In the 6 month follow-up, AF recurrence was associated only with total ablation time only. However, during the 1-year and 2-year follow-up periods, the presence of hypertension, impaired left atrial (LA) emptying fraction (eF) ($\leq 20\%$), decreased LA appendage (LAA) emptying velocity (≤ 20 cm/sec), and LAAeF ($\leq 20\%$) were correlated with AF recurrence (odds ratio [OR] = 1.87, 2.45, 1.93, and 2.15 respectively, $P = 0.016$, 0.004, 0.029, and 0.004 respectively). Among these factors, impaired LAeF was the only independent predictor of AF recurrence in multivariate analysis (OR = 2.81, $P = 0.012$).

In patients with persistent AF who had undergone RFCA, the best predictor of AF recurrence after ablation varied according to the follow-up period. Diminished LA function was the only predictor of recurrence in the 2-year follow-up. Pre-procedural assessment of LA function might be helpful in selecting those patients who would benefit from RFCA. (Int Heart J 2014; 55: 312-318)

Key words: Atrial fibrillation recurrence, Left atrial function, Radiofrequency catheter ablation, Echocardiographic predictors

Radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) has evolved as an effective therapeutic option in the last decade. RFCA is considered to be a potentially curative treatment to restore sinus rhythm (SR) by eliminating the focus of arrhythmia and modifying the left atrial (LA) structural substrate of AF. However, the recurrence rate after RFCA remains unsatisfactory (15% to $\geq 50\%$) depending on the ablation strategy and the type of AF.^{1,2} RFCA is an expensive procedure with potentially critical complications.³ Thus, it is crucial to identify those patients who are most likely to benefit from AF ablation with respect to restoration of the SR. Several clinical parameters, biomarkers, and imaging parameters have been reported to predict AF recurrence after RFCA. The reported predictors of recurrence after ablation are the presence of hypertension, long duration of AF, prolonged procedural time, enlarged LA diameter (LAD), or increased LA volume (LAV) and decreased LA function.⁴⁻⁹ However, there is no consensus regarding the risk factors for recurrence

because of heterogeneities in the study population, differences in the follow-up period, and differences in the type of AF.

Echocardiography has a well-recognized and essential role in the current guidelines for the assessment of cardiac structure and function in patients with AF.¹⁰ Several echocardiographic parameters for predicting the maintenance of SR after cardioversion, including LA size, mitral A wave velocity, and left atrium and LA appendage (LAA) mechanical function¹¹⁻¹³ have been reported. However, these echocardiographic predictors of AF recurrence have only been evaluated during a relatively short-term follow-up period. Moreover, the study population was not homogenous across the studies.

The purpose of this study was to investigate the clinical and echocardiographic predictors of AF recurrence after RFCA according to differences in the follow-up period in non-paroxysmal AF patients.

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This study received a research grant from Boryung Pharmaceutical Company in Seoul, Korea.

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Received for publication December 11, 2013. Revised and accepted February 3, 2014.

Released in advance online on J-STAGE June 5, 2014.

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METHODS

Study population: The study population consisted of 130 patients with non-valvular persistent AF who were initially cardioverted with catheter ablation between May 2008 and July 2010. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were performed within 24 hours before the procedure. After catheter ablation of AF, the patients were followed-up every 2 weeks during the first month and every 2-3 months for 2 years. At each hospital visit, the patient's medical history was taken and ECG was performed. Twenty-four hour ECG monitoring was performed during each visit for 1 year after RFCA and when symptoms occurred. Anti-arrhythmic drugs were prescribed during a blanking period of 3 months after RFCA. Recurrence was defined as atrial tachycardia lasting over 30 seconds and the detection of AF by ECG or 24-hour ECG monitoring during follow-up. Patients with significant valvular heart disease, hypertrophic cardiomyopathy, congenital heart disease, or a previous ablation procedure for AF were excluded from the study. This study was approved by the institutional review board of Korea University College of Medicine.

Echocardiography: Each patient underwent complete two-dimensional and Doppler echocardiography studies using commercially available equipment (Vivid 7; General Electric Medical Health, Waukesha, WI, USA and iE 33; Philips Medical, Andover, MA, USA). Standard echocardiographic examinations were performed according to the recommendations of the American Society of Echocardiography. Using M mode echocardiography, the left ventricular (LV) systolic and diastolic dimensions, LV end-diastolic wall thicknesses, and LA anteroposterior diameter were measured. LV ejection fraction (LVEF) was calculated by measuring the systolic and diastolic LV volumes using the modified biplane Simpson method. LV mass (LVM) was calculated using the Devereux-modified American Society of Echocardiography cube formula. Left atrial volume (LAV) was measured using the biplane area-length method. LA emptying fraction (eF) was calculated as $[(\text{LA maximal volume} - \text{LA minimal volume}) / \text{LA maximal volume}] \times 100$, as previously reported.¹⁴⁾ The LVM and LAV were indexed to the body surface area for correction (LVMI, LAVI). TEE was performed using the iE33 ultrasound machine (Philips Medical Systems) on the same day as TTE. LAA emptying and filling velocities were measured 1 cm below the orifice of the LAA. Maximal and minimal LAA areas were determined by manual tracing of the LAA endocardial border starting from the top of the limbus of the left upper pulmonary vein at end systole and end diastole as described previously. LAA emptying fraction (LAAeF) was calculated as $(\text{maximal area} - \text{minimal area}) / \text{maximal area} \times 100$.¹⁵⁾ Next, the presence of thrombus and spontaneous echo contrast (SEC) in the LA and LAA was checked. All echocardiographic measurements were performed in 5 RR intervals and were averaged.

Catheter ablation procedure: All patients provided written informed consent for enrollment in the study. Each patient was in a fasting, sedative state, and underwent electrophysiological studies and catheter ablation. Vascular access was obtained through both femoral veins. A double transseptal puncture was performed under fluoroscopic guidance to obtain access to the left atrium, and systemic anticoagulation was achieved with intravenous heparin to maintain an activated clotting time of

350-400 seconds. Pulmonary vein angiographic computed tomography and three-dimensional reconstruction were performed and electro-anatomic mapping was performed to guide ablation, using an image integration module (NavX; St Jude Medical, St. Paul, MN, USA and CARTO; Biosense Webster, Diamond Bar, CA, USA). A quadripolar catheter was placed in the ascending aorta as a temporal reference. A 5 F decapolar catheter (Torqr; inter-electrode spacing of 2-5-2 mm; Medtronic Inc., Minneapolis, MN, USA) was inserted into the coronary sinus. All patients underwent stepwise ablation. Circumferential ablation of 4 pulmonary vein ablation was performed using a 3.5 mm irrigated-tip catheter (NaviStar Thermocool, 7.5 Fr., D-curve; Biosense Webster), guided by a 20-pole Lasso deflectable mapping catheter (Biosense Webster). The circular mapping catheter was positioned close to the pulmonary vein ostium, and point-by-point radiofrequency ablation was performed to encircle the right and left pulmonary veins. Radiofrequency energy was applied in a power-controlled mode with a power limit of 30 W and a maximal temperature of 45°C. At each point, a radiofrequency current was applied until a voltage of < 0.1 mV was achieved, with a maximum of 60 seconds per point. The endpoint of pulmonary vein isolation was confirmed using entrance and exit blocks. If AF persisted after pulmonary vein isolation, complex fractionated atrial electrogram (CFAE) ablation was added according to the need to terminate AF. Electrogram-guided ablation was performed at all sites displaying CFAE, as defined previously.¹⁶⁾ The endpoint of electrogram-guided ablation was a significant reduction in the complex fractionated electrogram amplitude (> 80%), electrical silence, or organization to atrial tachycardia.

Statistical analyses: Quantitative data are expressed as the mean $\pm$ SD and categorical data are expressed as number or percentage. The chi-square test was used to evaluate differences in proportions in the maintenance SR and recurrence groups. One-way-analysis of variance (ANOVA) was used to compare continuous variables. To compare the maintenance SR and recurrence groups, Bonferroni post-hoc analysis was used. Univariate Cox regression was used to evaluate the echocardiographic parameters as potential predictors of outcome after ablation. Multivariate analysis was performed using the Cox regression test to determine the independent predictors of AF recurrence. Those variables with $P < 0.1$ in the univariate model were evaluated using multivariate analysis. To investigate the predictors of AF recurrence, LAVI and LA functional parameters were categorically analyzed. Increased LAV was defined as $\text{LAVI} \geq 34 \text{ mL/m}^2$ and impaired LAeF was defined as $\text{LAeF} \leq 20\%$. Decreased LAA emptying velocity and LAAeF were defined as $\text{LAA emptying velocity} \leq 20 \text{ cm/s}$ and $\text{LAAeF} \leq 20\%$, respectively. The criteria for increased LAVI, impaired LAeF, decreased LAA emptying velocity, and decreased LAAeF were categorized according to the published values of previous studies.^{5,17-19)} The predictive values for AF recurrence, including LAVI, LAeF, LAA emptying velocity, and LAAeF were tested using receiver operating characteristic (ROC) curve analysis. The sensitivities and specificities of each echocardiographic value were measured in the study population. A significant risk was determined if the 95% confidence interval (95% CI) exceeded 1, and the P -value was < 0.05. The percentage of patients free from AF recurrence was presented in a Kaplan-Meier survival curve. All analyses were

Table I. Clinical Characteristics of Study Population (*n* = 130)

	SR maintenance (<i>n</i> = 69)	AF Recurrence During 24 months (<i>n</i> = 61)	<i>P</i> [*]	6 months (<i>n</i> = 27)	6 to 12 months (<i>n</i> = 15)	12 to 24 months (<i>n</i> = 19)	<i>P</i> [†]
Age (years)	53.9 ± 9.1	55.7 ± 9.1	0.31	53.8 ± 10.7	59.0 ± 9.4	53.8 ± 6.4	0.44
Male, <i>n</i> (%)	61 (91.0%)	51 (44.7%)	0.14	23 (82.1%)	15 (88.2%)	15 (83.3%)	0.49
AF duration (months)	70.9 ± 62.0	88.3 ± 73.8	0.56	89.5 ± 57.5	97.6 ± 110.6	73.3 ± 32.1	0.49
Ablation time (minute)	143.5 ± 51.2	156.4 ± 50.0	0.09	177.4 ± 48.3 [‡]	134.6 ± 41.0	139.9 ± 52.7	0.03 [‡]
Comorbidity, <i>n</i> (%)							
Hypertension	22 (32.8%)	30 (49.2%)	0.05 [‡]	16 (57.1%)	8 (53.3%)	6 (31.6%)	0.32
Diabetes Mellitus	5 (7.5%)	2 (3.3%)	0.28	0	1 (6.6%)	2 (10.5%)	0.43
Congestive heart failure	5 (7.5%)	34 (6.6%)	0.73	1 (3.6%)	2 (13.3%)	1 (5.2%)	0.46
Previous stroke or TIA	5 (7.5%)	8 (13.1%)	0.57	3 (10.3%)	0	5 (26.3%)	0.07
Medication, <i>n</i> (%)							
ACEi or ARB	27 (40.3%)	30 (49.2%)	0.29	15 (53.6%)	8 (53.3%)	7 (36.8%)	0.65
Beta blocker	21 (31.3%)	24 (39.3%)	0.58	12 (42.9%)	6 (40.0%)	6 (31.6%)	0.80
Calcium channel blocker	13 (19.4%)	15 (24.6%)	0.52	9 (32.1%)	3 (20.0%)	3 (15.8%)	0.35
Statins	8 (11.9%)	12 (19.7%)	0.47	6 (21.4%)	2 (13.3%)	4 (21%)	0.58
Antiarrhythmic drug							
Class IC drug	26 (28.8%)	25 (39.3%)	0.98	13 (46.4%)	7 (46.7%)	5 (26.3%)	0.75
Digitalis	3 (4.5%)	2 (3.3%)	0.75	1 (3.7%)	1 (6.6%)	0	0.68
Amiodarone	37 (55.2%)	35 (57.3%)	0.94	13 (46.4%)	11 (57.9%)	11 (68.8%)	0.49

AF indicates atrial fibrillation; TIA, transient ischemic attack; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; *P*^{*}, *P* between with the maintenance SR group (*n* = 68) and AF recurrence group during 24 months (*n* = 61); and *P*[†], *P* between the AF recurrence groups according to recurrence time. Data are presented as mean ± SD or as numbers (percent). [‡]*P* ≤ 0.05, [§]*P* ≤ 0.05 between patients with maintenance of sinus rhythm and patients with AF recurrence within 6 months after ablation.

performed using the SPSS 12.0 software program (SPSS, Chicago, IL, USA).

RESULTS

Clinical characteristics: The clinical characteristics of the study population are summarized in Table I. The mean age of the subjects was 54.6 ± 9.3 years and 114 (87.6%) were men. The mean duration of AF was 77.4 ± 66.2 months. During the ablation procedure, each patient underwent isolation of 4 pulmonary veins. Additionally, CFAE-guided ablation was performed in 83 patients (64%). The median follow-up period was 33 months (range, 24–52 months) after ablation. Sixty-one patients (46.6%) had an AF recurrence during the 2 year period after ablation. Among the 61 patients with recurrence, 31 underwent repeat ablation for AF ablation during follow-up. Recurrences occurred within 6 months in 27 patients and two-thirds of all recurrences (42 patients, 31.5%) occurred within 1 year after ablation. There were no statistically significant differences in age and sex between the patients with and without AF recurrence. At each follow-up period, the durations of AF were also similar between the two groups. At 6 months after ablation, the total ablation time was significantly longer in patients with recurrent AF than in patients who maintained SR. These differences in ablation time between patients who developed AF recurrence and those who maintained SR did not persist at the 1- and 2-year follow-ups. In the entire patient population, the presence of hypertension was higher in the recurrence group than in the group without recurrence (49.2% versus 32.8% *P* = 0.05). There was no difference in medication between the AF recurrence group and the SR maintenance group and between the groups according to the follow-up periods (Table I).

Echocardiographic findings: There were no differences in the

LVMI and LVEF between patients who had recurrent AF and those who maintained SR. LAVI was higher in patients who had recurrent AF during the 2-year follow-up than that in patients with maintained SR (39.3 ± 12.0 mL/m² versus 35.0 ± 12.6 mL/m², *P* = 0.05). At the same time, LAeF was more impaired in patients with recurrent AF than in patients with maintenance SR (28.1 ± 7.7% versus 31.3 ± 9.4%, *P* = 0.034). In patients with recurrent AF, there were no differences in the LAVI and LAeF between the groups according to the timing of recurrence (Table II). In TEE parameters, the means of LAA velocities were significantly lower in patients with recurrence than in those with maintenance SR (emptying velocity; 28.9 ± 12.6 cm/s versus 36.8 ± 14.0 cm/s, *P* = 0.001, filling velocity; 36.1 ± 17.8 cm/s versus 47.3 ± 21.1 cm/s, *P* = 0.001). In addition, the LAAeF was lower in patients with AF recurrence than in those with maintenance SR (25.2 ± 11.9% versus 29.5 ± 11.1%, *P* = 0.017). The presence of SEC was more frequent in the AF recurrence group than in the maintenance SR group (52.7% versus 28.8%, *P* = 0.01). However, there were no differences in the LAA functional parameters and the presence of SEC between the three AF recurrence groups according to duration of the follow-up periods (Table II).

Differences in the predictor of AF recurrence after RFCA according to follow-up periods: Among the clinical factors, only total ablation time was predictive for AF recurrence at 6 months after ablation, which was evaluated using univariate Cox regression analysis (OR 1.013, 95% CI 1.003 - 1.022, *P* = 0.007). The presence of hypertension was associated with AF recurrence at the 1- and 2-year follow-ups using univariate Cox regression analysis (Supplementary Table).

To detect echocardiographic predictors of AF recurrence, patients were categorized into two groups according to the previously reported cutoff points of LA functional parameters. Increased LAV (LAVI ≥ 34 mL/m²)⁵⁾ was observed in 72 patients (55%), impaired LAeF (≤ 20%)¹⁷⁾ in 18 patients (13.8%), de-

Table II. Echocardiographic Variables of Study Population ($n = 130$)

	SR maintenance ($n = 69$)	AF Recurrence During 24 months ($n = 61$)	P^*	6 months ($n = 27$)	6 to 12 months ($n = 15$)	12 to 24 months ($n = 19$)	$P^†$
LVEF (%)	52.1 $\pm$ 7.3	53.1 $\pm$ 5.9	0.420	53.0 $\pm$ 5.6	52.9 $\pm$ 5.8	53.9 $\pm$ 6.6	0.81
LVMI (g/m ²)	113.5 $\pm$ 25.6	116.9 $\pm$ 20.5	0.366	117.1 $\pm$ 20.5	115.2 $\pm$ 22.9	117.4 $\pm$ 18.4	0.88
LA AP diameter (mm)	42.3 $\pm$ 5.5	43.1 $\pm$ 5.2	0.336	43.5 $\pm$ 4.4	42.5 $\pm$ 6.5	43.0 $\pm$ 6.0	0.84
LAVI (mL/m ²)	35.2 $\pm$ 12.6	39.3 $\pm$ 12.0	0.05 [‡]	39.7 $\pm$ 10.9	39.4 $\pm$ 12.8	38.6 $\pm$ 13.5	0.95
LAAeF (%)	31.4 $\pm$ 9.4	28.1 $\pm$ 7.7	0.034 [‡]	26.5 $\pm$ 6.6	27.5 $\pm$ 7.6	29.3 $\pm$ 7.0	0.45
E velocity (m/s)	0.069 $\pm$ 0.015	0.070 $\pm$ 0.0180	0.608	0.073 $\pm$ 0.019	0.067 $\pm$ 0.017	0.070 $\pm$ 0.017	0.59
DT (ms)	159.8 $\pm$ 35.9	163.8 $\pm$ 31.6	0.539	165.0 $\pm$ 34.6	161.8 $\pm$ 33.1	164.2 $\pm$ 24.8	0.82
E/e'	8.6 $\pm$ 2.7	9.3 $\pm$ 3.3	0.175	9.7 $\pm$ 3.4	9.1 $\pm$ 3.7	8.8 $\pm$ 2.9	0.67
LAA emptying velocity (cm/s)	36.6 $\pm$ 14.1	28.9 $\pm$ 12.6	0.001 [‡]	27.4 $\pm$ 12.7	30.8 $\pm$ 13.8	29.5 $\pm$ 11.8	0.53
LAA filling velocity (cm/s)	46.9 $\pm$ 21.0	36.1 $\pm$ 17.8	0.001 [‡]	35.7 $\pm$ 16.8	37.3 $\pm$ 17.6	38.1 $\pm$ 15.7	0.84
LAAeF (%)	29.5 $\pm$ 11.1	25.2 $\pm$ 11.9	0.017 [‡]	23.1 $\pm$ 12.4	29.2 $\pm$ 14.1	28.3 $\pm$ 12.5	0.08
The presence of SEC, n (%)	19 (28.8%)	29 (52.7%)	0.010 [‡]	17 (60.7%)	6 (35.3%)	10 (55.6%)	0.17

LVEF indicates left ventricular ejection fraction; LVMI, left ventricular mass index; LA AP diameter, left atrial anteroposterior diameter in M-mode; LAVI, left atrial volume, LAVI, left atrial volume index; LAAeF, left atrial emptying fraction, E velocity, peak early diastolic transmitral flow velocity, DT, deceleration time of E wave, E', peak early diastolic mitral annulus velocity; LAA, left atrial appendage; LAA eF, left atrial appendage emptying fraction; SEC, spontaneous echo contrast; P^* , P between group with maintenance SR ($n = 68$) and AF recurrence group during 24 months ($n = 61$); and $P^†$, P between AF recurrence groups by recurrence time. $^{\ddagger}P \leq 0.05$ between patients with maintenance SR and total patients with recurrence during 24 months.

Table III. The Area Under Curves and Criteria Values of ROC Curves of Echocardiographic Parameters for Recurrence of AF

	AUC	P	Cut-off value	Sensitivity	Specificity
LAVI	0.613	0.023	34 mL/m ²	67	54
LAAeF	0.632	0.008	20%	69	84
LAA emptying velocity	0.793	< 0.001	20 cm/s	61	82
LAAeF	0.672	0.0004	20%	50	73

LAVI, indicates left atrial volume index; LAAeF, left atrial emptying fraction; LAA, left atrial appendage; and LAA eF, left atrial appendage emptying fraction.

creased LAA emptying velocity (≤ 20 cm/s)¹⁹) in 24 patients (18.3%), and decreased LAAeF ($\leq 20\%$)¹⁸) in 40 patients (30.5%). Using univariate analysis, increased LAVI, impaired LAAeF, decreased LAA emptying velocity, and decreased LAAeF were identified as risk factors for AF recurrence at the 1-year follow up. The parameters to predict AF recurrence at the 2-year follow-up were similar to the risk factors at the 1-year follow-up, except for increased LAVI, using univariate Cox regression analysis (Supplementary Table). The sensitivity and specificity of each parameter to predict AF recurrence in the study population are summarized in Table III.

Multivariate Cox regression analysis by combining clinical and echocardiographic parameters was performed and ablation time remained as a risk factor for AF recurrence at the 6-month follow-up (OR 1.013, 95% CI 1.00 - 1.03, $P = 0.05$). However, at the 1- and 2-year follow-up, only impaired LAAeF remained as the single independent predictor of AF recurrence (1-year follow-up: OR 2.609, 95% CI 1.04 - 6.53, $P = 0.041$; 2-year follow-up: OR 2.662, 95% CI 1.99 - 5.92, $P = 0.016$).

Kaplan-Meier curves showed a significant difference in the SR maintenance rate between patients with impaired LAAeF and those with a relatively preserved LAAeF (Figure). Twenty-nine percent of the patients with preserved LAAeF had AF recurrence at the 1-year follow-up. However, in patients with impaired LAAeF, AF recurrence occurred in more than half of them (58.8%) during the 1-year period after RFCA. At the 2-year follow-up, less than 25 percent of patients with impaired LAAeF (21.3%) maintained SR, whereas 57.5% of pa-

Figure. Kaplan-Meier curves comparing the probability of maintaining sinus rhythm in patients with LAAeF > 20% and patients with LAAeF $\leq 20\%$.

tients with preserved LAAeF maintained SR during the 2 years after RFCA.

DISCUSSION

The present study was performed to evaluate the clinical and echocardiographic predictors of AF recurrence according to the follow-up periods after ablation. The main findings of

Table IV. Prediction of AF Recurrence After RFCA at one Year and Two Year by Multivariate Cox Regression Analysis ($n = 130$)

	Recurrence at 6 months			Recurrence at 1 year			Recurrence at 2 year		
	OR	95%, CI	P	OR	95%, CI	P	OR	95%, CI	P
Hypertension	1.121	0.348-3.609	0.848	1.290	0.555-3.002	0.554	1.409	0.698-2.842	0.338
Ablation time	1.013	1.000-1.025	0.05*	1.003	0.995-1.012	0.466	1.002	0.995-1.009	0.577
Increased LAV	0.515	0.137-1.934	0.325	0.874	0.349-2.189	0.773	0.871	0.403-1.881	0.725
Impaired LAeF	1.609	0.515-5.027	0.413	2.609	1.042-6.531	0.041*	2.662	1.197-5.920	0.016*
Decreased LAA emptying velocity	0.974	0.227-4.176	0.972	0.996	0.322-3.081	0.995	0.855	0.324-2.257	0.752
Decreased LAAeF	1.777	0.188-16.78	0.616	1.993	0.537-7.401	0.303	1.655	0.572-4.789	0.353
Presence of SEC	0.515	0.137-1.934	0.325	0.874	0.349-2.189	0.773	0.871	0.403-1.881	0.725

OR indicates odds ratio; and 95% CI, 95%, confidence interval. * $P \leq 0.05$.

our study were that the predictor of AF recurrence after RFCA varied according to the follow-up period and that intact pre-procedural LA function was correlated with longer maintenance of SR after RFCA in non-paroxysmal AF patients. The results of this study suggest that pre-procedural echocardiographic estimation of LA function might provide long-term prognostic information and might be helpful in selecting a therapeutic strategy for patients with non-paroxysmal AF.

RFCA has evolved in the past decades as an important therapeutic option for curing AF. However, AF recurrence after ablation remains a problem in a substantial number of patients. In this study population, the SR maintenance rate 2 years after RFCA was 53%. Several predictors of AF recurrence after ablation have been reported. However, there is no conclusive consensus, because of heterogeneities in the study population, differences in the follow-up period, and differences in the type of AF across studies. In the present study, the study population was limited to patients with non-paroxysmal AF, and each patient was followed-up at least 2 years after RFCA. The data were analyzed according to the follow-up period. During a relatively short-term follow-up period, at 6 months, prolonged ablation time was the only predictor of AF recurrence after ablation. However, impaired LAeF was the single independent predictor of AF recurrence at 1 and 2 years after catheter ablation. The reported clinical risk factors or echocardiographic parameters such as presence of hypertension, long duration of AF, enlarged LAD, or increased LAV were not predictive of AF recurrence in the subjects of this study.

Prolonged ablation time has been reported to be related to AF recurrence in a previous study.²⁰ However, in the present study, longer ablation time was correlated with recurrence only for a short-term follow-up period. It is not clear whether longer AF ablation time itself might be a pro-arrhythmogenic factor or if it is required for ablation of a remodeled LA with multiple AF foci. Atrial tissue edema after RFCA has been reported to be related with early AF recurrence.²¹ As the presence of tissue edema may prevent achieving sufficient energy to induce myocardial necrosis, electrical isolation between the LA and the pulmonary vein by RFCA could not be achieved effectively. Therefore, a longer ablation time could result in increased tissue edema, hence, longer ablation time was associated with AF recurrence in the short-term after ablation. Moreover, the finding that prolonged ablation time was an independent risk factor of early AF recurrence suggests that subtle structural and functional abnormality of LA could exist. The marginally impaired LAAeF in patients of the early recurrence group than in patients of the 1- and 2-year recurrent groups supports the above explanation. This can be proved by increasing the number of

study patients. Moreover, experimental studies have suggested that AF induced atrial fibrosis and its pathological changes might induce reduced global LA function. A more sophisticated method, such as cardiac magnetic resolution, can be used to prove the relation between early anatomical and functional change of the left atrium.

Using the mitral annular velocity, impaired LA function has been reported to be an independent risk factor of AF recurrence in patients with paroxysmal AF.²² Recently, several study groups attempted to clarify the value of LA function to predict AF recurrence using LA deformation imaging in patients undergoing either cardioversion^{23,24} or ablation procedures.^{8,9,25} In some previous studies, deteriorated LA global strain was suggested to be a risk factor for AF recurrence after ablation.^{9,26} LAeF was used in our study and it is a generally accepted representative of LA reservoir function, similar to LA global strain. Therefore, the result of our study agrees with that of previous studies. However, study subjects in previous studies comprised patients with paroxysmal and non-paroxysmal AF and the number of those with non-paroxysmal AF was relatively small. Furthermore, deformation images of the LA, such as strain and strain rate, have several clinical limitations. It is not possible to simultaneously evaluate LA function during image acquisition and intra- and inter-observer variability is high. In this study, the subjects were limited to a large population of patients with nonparoxysmal AF. In addition, the method for evaluating LA function (ie, measurement of LAeF), is relatively simple and clinically feasible. LAeF can be simultaneously measured while performing TTE.

LA enlargement caused by abnormal LV diastolic dysfunction or because of structural remodeling due to AF could promote the occurrence of AF. Therefore, increased LAD and LAV, as representative measures of LA size, were evaluated as predictors of AF recurrence after RFCA in previous studies. Some studies demonstrated that an increased LAD was an independent predictor of AF recurrence⁴ and in a meta-analysis of the previous report, an increased LAD ≥ 50 mm was a predictor of AF recurrence.⁶ However, in this study population, there was no significant difference in LAD between the AF recurrence and SR maintenance groups and increased LAD was not correlated with AF recurrence. LAD measured on the M-mode echocardiogram could not accurately represent the actual LA size, and LAV and LAVI have been reported to be better indices of LA size than LAD. Several studies measured LAV and showed the relation of increased LAV with the AF recurrence after ablation. In this study also, using univariate analysis, an increased LAV was correlated with AF recurrence during the 1-year follow-up. However, in multivariate analysis an

increased LAV was not an independent predictor of AF recurrence. The reason for these results is not clear. The LAVI in the present study population was smaller than that in a previous study.⁵⁾ It may be because physicians non-randomly selected patients who will benefit from the ablation therapy procedure, and might have excluded patients with a huge left atrium. Another possible explanation is that the present study included patients in a relatively earlier stage of atrial remodeling than those of the other study populations. In addition, it might be possible that Asian people generally have a smaller LA than Caucasians.²⁷⁾ For this reason, no statistical significance was observed in LAVI between patients with and those without recurrence.

Berruezo, *et al* demonstrated that a history of hypertension was an independent predictor of AF recurrence after catheter ablation during a 13-month follow-up.⁴⁾ Hypertension is the most prevalent risk factor for AF occurrence in the general population.²⁸⁾ Impaired diastolic function in a hypertensive heart imposes increased afterload to the LA and results in LA stretching, enlargement, and fibrosis.⁴⁾ The presence of hypertension was also associated with AF recurrence in ≥ 1 -year follow-up in this study. However, hypertension was not an independent risk factor for AF recurrence after catheter ablation in multivariate analysis. This result suggests that LA functional impairment as a complication of hypertension may be an important risk factor for AF, and not merely the presence of hypertension.

The present study has several limitations. One major limitation is the method of evaluating LA function. Calculation of LAeF by measuring end-systolic and end diastolic LAV was time-consuming and may be variable due to the diverse R-R interval in AF. To improve accuracy, we averaged 5 consecutive beats. The other limitation is that LAeF could be influenced by the volume status and heart rate. Nevertheless, all measurements were done when patients were in a stable condition. LAV was measured when the heart rate was < 120 beats per minute. Therefore, the volume status and heart rate may not be major confounding factors for LAeF.

In conclusion, our study demonstrated that the predictors of recurrence after RFCA were different depending on the follow-up period. At the 6-month follow-up, ablation time was the most important factor for recurrence, whereas pre-procedural LA function was the most important factor during the 1-year follow-up. The heterogeneity of risk factors for AF recurrence after ablation in previous studies may be partly due to different follow-up periods. Evaluation of LA function by routinely performing echocardiography may aid in selecting patients who would maintain SR for a long time after a successful catheter ablation. However, this finding needs to be confirmed by large-scale randomized prospective studies.

REFERENCES

- Chinitz JS, Halperin JL, Reddy VY, Fuster V. Rate or rhythm control for atrial fibrillation: update and controversies. *Am J Med* 2012; 125: 1049-56. (Review)
- Thomas SP, Sanders P. Catheter ablation for atrial fibrillation. *Heart Lung Circ* 2012; 21: 395-401. (Review)
- Cappato R, Calkins H, Chen SA, *et al*. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010; 3: 32-8.
- Berruezo A, Tamborero D, Mont L, *et al*. Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation. *Eur Heart J* 2007; 28: 836-41.
- Shin SH, Park MY, Oh WJ, *et al*. Left atrial volume is a predictor of atrial fibrillation recurrence after catheter ablation. *J Am Soc Echocardiogr* 2008; 21: 697-702.
- D'Ascenzo F, Corleto A, Biondi-Zoccai G, *et al*. Which are the most reliable predictors of recurrence of atrial fibrillation after transcatheter ablation?: a meta-analysis. *Int J Cardiol* 2013; 167: 1984-9.
- von Bary C, Dornia C, Eissnert C, *et al*. Predictive value of left atrial volume measured by non-invasive cardiac imaging in the treatment of paroxysmal atrial fibrillation. *J Interv Card Electrophysiol* 2012; 34: 181-8.
- Schneider C, Malisius R, Krause K, *et al*. Strain rate imaging for functional quantification of the left atrium: atrial deformation predicts the maintenance of sinus rhythm after catheter ablation of atrial fibrillation. *Eur Heart J* 2008; 29: 1397-409.
- Hammerstingl C, Schwekendiek M, Momcilovic D, *et al*. Left atrial deformation imaging with ultrasound based two-dimensional speckle-tracking predicts the rate of recurrence of paroxysmal and persistent atrial fibrillation after successful ablation procedures. *J Cardiovasc Electrophysiol* 2012; 23: 247-55.
- Fuster V, Rydén LE, Cannom DS, *et al*. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation* 2006; 114: e257-354.
- Okcu B, Yigit Z, Arat A, Baran T, Küçükoglu MS. Stunning of the left atrium after conversion of atrial fibrillation: predictor for maintenance of sinus rhythm? *Echocardiography* 2005; 22: 402-7.
- Park MY, Shin SH, Oh WJ, *et al*. Prognostic implication of the left atrial appendage mechanical reserve after cardioversion of atrial fibrillation. *Circ J* 2008; 72: 256-61.
- Park SM, Kim YH, Choi JJ, Pak HN, Kim YH, Shim WJ. Left atrial electromechanical conduction time can predict six-month maintenance of sinus rhythm after electrical cardioversion in persistent atrial fibrillation by Doppler tissue echocardiography. *J Am Soc Echocardiogr* 2010; 23: 309-14.
- Borg AN, Pearce KA, Williams SG, Ray SG. Left atrial function and deformation in chronic primary mitral regurgitation. *Eur J Echocardiogr* 2009; 10: 833-40.
- Pollick C, Taylor D. Assessment of left atrial appendage function by transesophageal echocardiography. Implications for the development of thrombus. *Circulation* 1991; 84: 223-31.
- Park JH, Pak HN, Kim SK, *et al*. Electrophysiologic characteristics of complex fractionated atrial electrograms in patients with atrial fibrillation. *J Cardiovasc Electrophysiol* 2009; 20: 266-72.
- Hudsmith LE, Petersen SE, Francis JM, Robson MD, Neubauer S. Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. *J Cardiovasc Magn Reson* 2005; 7: 775-82.
- Li YH, Lai LP, Shyu KG, *et al*. Clinical implications of left atrial appendage function: its influence on thrombus formation. *Int J Cardiol* 1994; 43: 61-6.
- Verma A, Marrouche NF, Yamada H, *et al*. Usefulness of intracardiac Doppler assessment of left atrial function immediately post-pulmonary vein antrum isolation to predict short-term recurrence of atrial fibrillation. *Am J Cardiol* 2004; 94: 951-4.
- Shim J, Joung B, Park JH, Uhm JS, Lee MH, Pak HN. Long duration of radiofrequency energy delivery is an independent predictor of clinical recurrence after catheter ablation of atrial fibrillation: over 500 cases experience. *Int J Cardiol* 2013; 167: 2667-72.
- Richter B, Gwechenberger M, Socas A, *et al*. Markers of oxidative stress after ablation of atrial fibrillation are associated with inflammation, delivered radiofrequency energy and early recurrence of

- atrial fibrillation. *Clin Res Cardiol* 2012; 101: 217-25.
22. Yoon JH, Moon J, Chung Hm, *et al.* Left atrial function assessed by Doppler echocardiography rather than left atrial volume predicts recurrence in patients with paroxysmal atrial fibrillation. *Clin Cardiol* 2013; 36: 235-40.
 23. Di Salvo G, Caso P, Lo Piccolo R, *et al.* Atrial myocardial deformation properties predict maintenance of sinus rhythm after external cardioversion of recent-onset lone atrial fibrillation: a color Doppler myocardial imaging and transthoracic and transesophageal echocardiographic study. *Circulation* 2005; 112: 387-95.
 24. Boyd AC, Schiller NB, Ross DL, Thomas L. Segmental atrial contraction in patients restored to sinus rhythm after cardioversion for chronic atrial fibrillation: a colour Doppler tissue imaging study. *Eur J Echocardiogr* 2008; 9: 12-7.
 25. Mirza M, Caracciolo G, Khan U, *et al.* Left atrial reservoir function predicts atrial fibrillation recurrence after catheter ablation: a two-dimensional speckle strain study. *J Interv Card Electrophysiol* 2011; 31: 197-206.
 26. Inaba Y, Yuda S, Kobayashi N, *et al.* Strain rate imaging for noninvasive functional quantification of the left atrium: comparative studies in controls and patients with atrial fibrillation. *J Am Soc Echocardiogr* 2005; 18: 729-36.
 27. Zhuang J, Wang Y, Tang K, *et al.* Association between left atrial size and atrial fibrillation recurrence after single circumferential pulmonary vein isolation: a systematic review and meta-analysis of observational studies. *Europace* 2012; 14: 638-45.
 28. Psaty BM, Manolio TA, Kuller LH, *et al.* Incidence of and risk factors for atrial fibrillation in older adults. *Circulation* 1997; 96: 2455-61.